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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LEWIS, PATRICK T	
ART UNIT	**PAPER NUMBER**
1623	9

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,847	GOLDSHTEIN, RINA	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *19-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 33-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-18 and 33-49) wherein the lipophilic compound/particle is a vitamin, antibiotic or hormone and wherein the amphiphilic polymer is a natural polysaccharide in Paper No. 8 dated April 11, 2003 is acknowledged.

2. Claims 19-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8 dated April 11, 2003.

Double Patenting

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claims 5, 8-10, 12-18, 43-44, and 46-49 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 20-22, 25-27, 29, 31, 32-33, 58-59, 61, 63, 65, and 66 of copending Application No. 10/256,023. This is a

provisional double patenting rejection since the conflicting claims have not in fact been patented.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-4, 6-7, 11, 33-42, and 45 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8-9, 11, 14-15, 24, 47-56, and 60 of copending Application No. 10/256,023 ('023). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-4 and 6-7 differ from claims 1, 8-9, 11, and 14-15 of the '023 application in that the instantly claimed invention is not limited to complexes wherein no valent bonds are formed; however, this limitation would have been obvious to one of ordinary skill in the art at the time of the invention as applicant states that a significant advantage of the instantly claimed complex is that no new bonds are formed. Claims 2 and 7 are narrower in scope with respect to the lipophilic particles complexed; however, the

invention of claims 2 and 7 is fully encompassed within the limitations of the '023 application.

Claim 11 differs from claim 24 of the '023 application in that the scope of lipophilic compounds are narrower (does not read upon "other compounds and/or intermediates"); however, the invention of claim 11 is fully encompassed within the limitations of claim 24.

Claims 33-42 differ from claims 47-56 of the '023 application in that the instantly claimed invention is not limited to complexes wherein no valent bonds are formed; however, this limitation would have been obvious to one of ordinary skill in the art at the time of the invention as applicant states that a significant advantage of the instantly claimed complex is that no new bonds are formed.

Claim 45 differs from claim 60 of the '023 application in that the scope of lipophilic compounds are narrower (does not read upon "other compounds and/or intermediates"); however, the invention of claim 45 is fully encompassed within the limitations of claim 60.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-18 and 33-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A written description analysis involves three principle factors:

1. Field of the invention and predictability of the art
2. Breadth of the claims
3. For each claimed species/genus, possession of claimed invention at the time of the filing.

Claims 1-7 are drawn to a hydrophobic inclusion complex comprising nano-sized water-insoluble lipophilic particles and an amphiphilic polymer or a method for producing said complex. Claims 8-18 and 33-49, drawn to a method for forming a hydrophilic inclusion complex comprising forming an emulsion comprising an amphiphilic molecule in an aqueous solvent and lipophilic compounds in a non-aqueous solution, forming nano-sized lipophilic particles in a nano-emulsion, and removing carrier solvent from nano-emulsion. Applicant has elected to have the invention examined wherein the lipophilic particles are vitamins, antibiotics, or hormones and wherein the amphiphilic polymer is a natural polysaccharide.

The breadth of the claims is such that any lipophilic vitamin, antibiotic, or hormone forms a complex with any natural polysaccharide. The specification discloses a table on page 19 showing a combination of water-phase, polymer, and lipophilic drug agent and the process temperature used for the preparation of selected nano-emulsions and their stability determined via length of time. Polymers disclosed in the table include

carragennan, xantan, polyacrylamide, starch and agar-agar. The table also lists lipophilic drug agents; however, it is unclear what is actually included in the resulting complex. For example, the entry wherein xantan is the polymer recites "Nut oil & almond oil (Oleum Amigdalarum) 1:1, aromatic esters' mixture, triglycerides, aromatic nitrile an vitamins" as the lipophilic drug agent. No guidance is provided beyond the table on page 19 regarding what lipophilic drug agents are useful for forming the instantly claimed complex. There is no disclosure, beyond the claims, of antibiotics or hormones complexed with a natural polysaccharide. The examples fail to provide further guidance as the procedure is only described in generic terms. The support in the specification is not adequate for the claim of the formation of a hydrophilic inclusion complex comprising forming an emulsion comprising an amphiphilic molecule in an aqueous solvent and lipophilic compounds in a non-aqueous solution, forming nano-sized lipophilic particles in a nano-emulsion, and removing carrier solvent from nano-emulsion.

The written description requirement for a claimed genus may be satisfied through sufficient description of an adequate representation of species by functional characteristics sufficient to show the applicant was in possession of the claimed genus. There are a variety of vitamins, antibodies, hormones, and polysaccharides, each with a certain degree of specificity in terms of molecular weight, functional group moieties, and chemical reactivity for which there is not seen adequate support for forming an inclusion complex in the instant disclosure. There is limited predictability in the art that any one polysaccharide is capable of forming inclusion complexes with any vitamin, hormone, or

antibody as broadly claimed. To provide adequate support for the breadth of the claims, applicant would have to provide sufficient evidence that a representative number of polysaccharides form inclusion complexes with a representative number of each member of the group consisting of vitamins, hormones, and antibodies. No data is presented showing an inclusion complex of a natural polysaccharide and a vitamin, hormone, or antibody. An adequate representation of species requires that the species which are expressly described and recognized in the art as representative of the entire genus. What constitutes a "representative number" is an inverse function of the predictability in the art in question. As such, there is not seen any data or correlative prior art evidence which supports applicant's claim that at the time of filing, that hydrophilic inclusion complex are produced comprising forming an emulsion comprising an amphiphilic molecule (natural polysaccharide) in an aqueous solvent and lipophilic compounds (vitamin, hormone, or antibody) in a non-aqueous solution, forming nano-sized lipophilic particles in a nano-emulsion, and removing carrier solvent from nano-emulsion.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rolfes et al. U.S. Patent 6,221,399 (Rolfes) in combination with Parikh et al. U.S. Patent 6,228,399 (Parikh).

Claims 1-7 are directed to a hydrophobic inclusion complex comprising nano-sized water-insoluble lipophilic particles and an amphiphilic polymer which surrounds said lipophilic particles. Claims 2-7 depend from claim 1. Claims 2-4 limit the nature of the lipophilic particles. Claim 5 limits the invention to complexes wherein the interaction of the lipophilic particles and amphiphilic polymer is via the formation of non-valent bonds. Claim 6 limits the invention to a water-soluble complex. Claim 7 limits the size of the lipophilic particles to 10-100 nanometers.

Rolfes teaches an interpolymer complex incorporating an active agent. Rolfes teaches vitamins and antibiotics as active agents incorporated into the interpolymer complex (column 8, lines 1-4). Polymers used to form the interpolymer complex include guar gum, cellulose and its derivatives, starches and their derivatives, and xanthan gum (column 8, lines 32-64). The complexation occurs via reversible physical molecular forces such as hydrogen bonding, hydrophobic interactions, van der Waals forces,

electrostatic- ionic- or Coulomb forces and combinations of these interactions excludes irreversible chemical forces such as covalent bonding (column 6, lines 46-51). Rolfes further teaches that the active agent may be dissolved, dispersed, suspended, emulsified or slurried together with the polymers in a mixture of solvents and/or liquid media (column 9, lines 17-37). Suitable solvents and liquid media include: water, alcohols, acetone, and mixtures thereof.

Rolfes differs from the instantly claimed invention in that Rolfes does not teach active agents as nano-sized; however, Parikh teaches this deficiency.

Parikh teaches that microparticles (particles having diameters of from nanometers to micrometers) provide some specific advantages over the unformulated non-micronized drug particles (column 1, lines 32-47). The advantages include improved oral bioavailability of drugs that are poorly absorbed from GI tract, development of injectable formulations that are currently available only in oral dosage form, less toxic injectable formulations that are currently prepared with organic solvents, sustained release of intramuscular injectable drugs that are currently administered through daily injection or constant infusion, and preparation of inhaled, ophthalmic formulation of drugs that otherwise could not be formulated for nasal or ocular use.

It would have been obvious to one of ordinary skill in the art at the time of the invention utilize nano-sized active agents to form the inclusion complex taught by Rolfes. One would have been motivated to do so based on the disclosure of Parikh which teaches specific advantages over the unformulated non-micronized drug particles.

Conclusion

12. Claims 1-49 are pending. Claims 1-18 and 33-49 are rejected. Claims 19-32 are withdrawn from further consideration as being drawn to a nonelected invention. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 10:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

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June 26, 2003